A simple prophylaxis regimen for MRSA: its impact on the incidence of infection in patients undergoing liver resection

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ABSTRACT

INTRODUCTION Methicillin-resistant *Staphylococcus aureus* (MRSA) infection has increased at an alarming rate in the recent past and has major cost implications. The aim of this study is to assess the impact of a policy of pre-operative MRSA prophylaxis on the incidence of MRSA infection in patients undergoing liver resection.

PATIENTS AND METHODS A total of 585 patients underwent hepatectomy in a tertiary referral centre between January 2000 and September 2005. In September 2003, a policy of MRSA prophylaxis (nasal mupirocin and triclosan wash for 5 days) was introduced within this unit. Demographic, pathological and outcome data were compared between the pre- and post-MRSA prophylaxis cohorts.

RESULTS The prevalence of MRSA infection prior to initiating the prophylaxis protocol was 29 patients (8.3%) and this fell to 9 patients (3.8%; $P = 0.029$). Furthermore, patients who had MRSA-related infection had a higher incidence of additional complications compared to the rest of the cohort ($P = 0.001$). Total cost savings incurred as a result of this protocol over the past 2 years has been approximated at £28,893.

CONCLUSIONS Introduction of a simple MRSA prophylaxis policy has had a significant reduction on the incidence MRSA-related infection within our patient population, leading to reduced morbidity and cost saving to the UK National Health Service.

KEYWORDS

Prophylaxis – Protocol – MRSA – Cost savings – Mupirocin

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Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a major cause of morbidity within the UK National Health Service. The cost implications of an aggressive control policy is significant in terms of financial implications as well as additional labour involvement.¹ Several authors have published favourable results showing a reduction in the incidence of MRSA carriage by adoption of a prophylaxis regimen.^{2–6} However, the exact role of a prophylaxis regimen on subsequent MRSA infection is unclear with conflicting data presented within the literature.^{7–9}

A previous study in our institution, conducted in orthopaedic patients, showed a significant reduction in the incidence of surgical-site infections following the adoption of a policy of empirical peri-operative prophylaxis using the combination of nasal mupirocin and a shower or bath with 2% triclosan.¹⁰ In response to these results, the hepatobiliary unit adopted a policy of MRSA prophylaxis for all patients undergoing elective major hepatobiliary procedures. The aim

of this study was to assess the impact of such prophylaxis on the incidence of MRSA-related infection.

Patients and Methods

This report details a retrospective longitudinal study of patients who underwent hepatectomy within this tertiary referral hepatobiliary unit from January 2000 to September 2005. The data were obtained from a prospectively collected surgical database and confirmed by medical records and patient reviews. The data examined included patient demographics, hospital stay and complications, MRSA infections and sites of MRSA colonisation as compiled by analysis of laboratory records.

Patients were not routinely screened for MRSA carriage in this unit, thus identification of MRSA was via diagnostic sampling of wound and drain sites as well as sampling of sputum, intravenous/urinary catheters and blood cultures

as indicated on clinical grounds. Diagnostic sampling occurred in response to the development of signs or symptoms possibly indicating infection: the protocol for such sampling did not change after implementation of MRSA prophylaxis. In September 2003, the unit initiated a protocol of MRSA prophylaxis for all patients undergoing elective major hepatobiliary procedures. The MRSA prophylaxis protocol consisted of mupirocin applied to the nose three times a day from the day of admission to the fifth postoperative day. Triclosan (2%) was also used twice daily, in a shower or bath, over the same period of time. The total cost of this regimen per patient was £5.40.

The cost implications of this prophylaxis protocol were calculated by initially estimating the rough cost per case of MRSA in terms of bed occupancy, use of antibiotics and dressings as well as district nursing care. This cost was then multiplied by the calculated numbers of MRSA cases prevented by the prophylaxis. Finally, the total cost of prophylaxis was subtracted enabling an estimation of the total savings incurred over the time-frame of the study. The daily cost of a ward bed within our institution is £250. The cost of intravenous vancomycin (used twice daily for a 10-day course) is £93 and dressings are a further £50. In addition, the cost of district nursing care, including dressings (based on an alternated daily visit for a 2-week period) is £350.

Statistical analysis

The SPSS v.9 statistical program was used to analyse the data. The chi-squared test was used to analyse any significant differences between the two cohorts of patients treated before and after introduction of the MRSA prophylaxis protocol. Otherwise, for continuous variables, the Mann-Whitney U-test was applied. The Wilcoxon signed rank test was used to compare hospital stay with timing of MRSA identification.

Results

Demographics and characteristics

A total of 585 patients were included in the study. The mean age at time of surgery was 64 years (range, 23–87 years). The pre-MRSA protocol cohort consisted of 348 patients compared to 237 in the post-MRSA protocol cohort. Differences in clinicopathological features between the pre- and post-MRSA protocol cohorts are presented in Table 1. These two patient populations were well matched, in terms of age, aetiology, gender and rate of tertiary referrals.

Outcome

There were 38 (6.5%) patients identified with MRSA-related infection during the study period. Of these, 34 (89.5%) patients had clinical evidence of surgical site infection with

Table 1 Patient demographics and pathological details

	Pre-protocol (%)	Post-protocol (%)
Demographics		
Age*	63	65
Male gender	198 (57)	140 (59)
Tertiary referral	235 (67)	179 (75)
Aetiology		
Colorectal metastases	239 (69)	178 (75)
Cholangiocarcinoma	29 (8)	14 (6)
Other malignancy	28 (8)	14 (6)
Hepatocellular carcinoma	26 (7.5)	14 (6)
Benign disease	26 (7.5)	17 (7)
Total	348	237

*Values represent median.

MRSA-positive wound-swab cultures. Of the remaining patients, three had evidence of intravascular catheter infection with positive blood cultures. Furthermore, one patient had clinical and radiological evidence of a chest infection with positive sputum cultures. The prevalence of MRSA-related infection in the pre-protocol cohort was 8.3% (29 patients). Following the introduction of the protocol, this fell to 3.8% (9 patients). This difference was statistically significant ($P = 0.029$; hazard ratio 0.56; 95% CI 0.31–1). As a result of this protocol, a projected number of 11 cases of MRSA-related infection were prevented within the prophylaxis cohort. The number of patients required to be treated in order to prevent one case of MRSA was, therefore, 22 patients.

Table 2 Postoperative complications pre- and post-implementation of MRSA protocol

Complication	Pre-protocol	Post-protocol
Bile leak	12	4
Wound infection	23	17
Liver failure/encephalopathy	20	6
Postoperative haemorrhage	11	3
Intra-abdominal sepsis	15	5
Chest infection	10	5
Others	4	2
Total number	95/315 (30%)	42/187 (22%)

The presence of complications was recorded in 502 (85.8%) patients. Of these, 137 (27.3%) developed complications. The incidence of complications in the pre-protocol cohort was 30% compared with 22% in the post-protocol cohort ($P = 0.071$; Table 2). Among patients with MRSA-related infection, however, 18 (47.3%) patients had additional complications that were not directly related to the presence of MRSA. The increased incidence of additional complications among patients with MRSA, when compared with those who did not have MRSA, was statistically significant ($P = 0.001$).

The median hospital stay for patients who developed MRSA infection was 20 days (mean, 21.5 ± 13.6 days) compared to 8 days (mean, 11.5 ± 29.9 days) for those who did not ($P = 0.001$). Among patients with MRSA-related infection, the median time to identification of MRSA from surgery was 6 days (mean, 15.1 ± 21.9 days). There was no significant difference comparing the hospital stay of non-MRSA patients and the time interval between surgery and isolation of MRSA ($P = 0.836$).

Cost implications

The cost incurred to prevent each new case of MRSA was £116 [$(237 \times £5.40)/11$]. Patients with MRSA infection had a higher incidence of unrelated complications that could also affect hospital stay, thus we excluded cases with complications other than wound infection. After excluding confounding variables, the mean hospital stay for patients with MRSA-related infection was 18.4 ± 14.3 days compared to 9.4 ± 29.9 days for all others ($P = 0.001$). Using this parameter, the crude financial cost incurred from each MRSA case was calculated at £2,743. In overall terms, the cost savings incurred by this protocol was £28,893 (Table 3).

Discussion

There have been several reports in the literature that have shown beneficial results for MRSA prophylaxis.^{2,5} These regimens, however, include the use of intravenous antibiotics, which incur significant cost implications. The use of topical mupirocin is relatively cost-effective and has been supported by several series.^{4,5,10} However, the number of patients in all these studies has been relatively small.^{4,5} In a review, the use of mupirocin ointment was found to be 97% effective in eradicating *S. aureus* nasal carriage.⁶ Also, carriers who received mupirocin before cardiothoracic or general surgery operations had almost 50% fewer *S. aureus* surgical-site infections.⁶ A meta-analysis of patients undergoing dialysis showed that the use of mupirocin reduced the rate of infection by 68%.⁷ However, these results have been challenged by a further meta-analysis⁸ which suggested that mupirocin use was associated with a reduction in MRSA nasal carriage but had little impact on rates of surgical

Table 3 Cost implications of MRSA infections

Total cost of the 11 MRSA cases prevented in protocol cohort	£30,173
Cost of prophylaxis protocol	£1,280
Total savings incurred	£28,893
Total saving per patient undergoing prophylaxis	£122

infection. Paterson *et al.*⁹ found mupirocin use (not specifically related to surgery) frequently (in 37% of cases) failed to prevent nasal *S. aureus* re-colonisation and did not prevent future MRSA infections among patients in a liver transplant unit. Our experience in Leeds using mupirocin-based peri-operative prophylaxis has shown that reductions in postoperative infection rates in orthopaedic patients were associated with significant and sustained reductions in the prevalence of nasal MRSA carriage.¹⁰

There are concerns that long-term use of mupirocin in this manner may promote resistance, which in turn may undermine its efficacy. However, short-term, non-repeated courses of mupirocin are less likely to induce resistance than prolonged and/or repetitive administration. Resistance emergence has been monitored in our institution and, to date, there have been no clinical failures of prophylaxis on the hepatopancreatobiliary unit caused by mupirocin-resistant strains of MRSA. In the orthopaedic unit in our institution, there has been no trend towards increased prevalence of mupirocin resistance during a 4-year follow-up period after implementation of similar peri-operative prophylaxis.¹¹

The current study consists of a large cohort of patients. The overall rate of infection within this patient population was 6.5% and this is comparable to the published literature.^{5,12} All patients from whom MRSA was isolated had clinical evidence of infection that in the majority of cases was a surgical-site infection. Given the retrospective nature of the study, it is difficult to ensure accuracy with respect to the diagnosis of infection. However, we emphasise that, as we do not collect screening samples (for MRSA or other pathogens), correlating the isolation of MRSA from a specimen with the diagnosis of infection is more straightforward. The pre- and post-protocol cohorts of patients were well matched in terms of patient demographics; however, as this study is retrospective in nature, data on variables such as ASA score, body mass index and the incidence of diabetes that may impact upon surgical site infection are unfortunately lacking. Prophylaxis was found to be associated with a significant reduction in the rate of MRSA-related infection ($P = 0.029$). The associated hazard ratio of 0.56 and

confidence interval are indicative of a significant reduction in MRSA-related infection rates.

A statistically significant association between the presence of complications, not directly attributable to MRSA and the identification of MRSA-related infection was noted. The reasons for this are unclear. This may be explained by the fact that patients who develop complications become immunocompromised and are thus more susceptible to prevalent pathogens such as MRSA. Furthermore, such complications may also result in other interventions associated with increased risk of acquisition and subsequent infection with MRSA. However, there was no significant difference in the incidence of surgical complications in the pre- and post-protocol cohorts. Thus, the presence of a complication *per se* was not felt to be a confounding factor for the reduction in the rate of MRSA-related infection.

The cost implications of MRSA infection are significant. We found that MRSA-related infection was associated with a prolonged hospital stay. Notably, the median time to identification of MRSA was less than the median hospital stay. This suggests that MRSA acquisition was associated with prolonging hospital stay, rather than a prolonged hospital stay leading to subsequent acquisition of MRSA. The calculated potential savings over the 2-year period since the prophylaxis protocol was initiated were £28,895. This may, however, be an underestimation of the total financial costs of MRSA as additional factors such as blood tests, intravenous fluids and other disposables, *etc.* have not been included in the cost analysis. Also, we did not estimate the socio-economic costs of infection. Furthermore, the psychological stress incurred to each patient who develops MRSA as well as the delay in treatment of others as a result of prolonged bed occupancy is difficult to quantify.

MRSA-related infection is an increasing concern; in response, the UK Department of Health launched nationwide initiatives in an effort to reduce hospital-related infection.¹⁵ These initiatives were only recent and, during the study period between January 2000 and September 2005, no wider trust initiatives were introduced which may have had an impact on MRSA-related infection rates.

Conclusions

Adoption of a simple peri-operative prophylaxis protocol has reduced the incidence of MRSA-related infection, resulting in reduction in patient morbidity and significant cost savings to our institution.

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